

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A mouse comprising in its genome a first exogenous DNA molecule that functionally disrupts a NFATp gene of said mouse and a second exogenous DNA molecule that functionally disrupts a NFAT4 gene of said mouse, wherein said mouse exhibits a non-wildtype phenotype characterized by increased Th2 cytokine production relative to a wildtype mouse.

2.-32. (Canceled)

33. (Currently Amended) The ~~transgenic~~ mouse of claim ~~1 32, 49, and 52~~, wherein the phenotype of said mouse is further characterized by lymphadenopathy ~~relative to a wild-type mouse~~.

34. (Currently Amended) The ~~transgenic~~ mouse of claim ~~1 32, 49, and 52~~, wherein the phenotype of said mouse is further characterized by splenomegaly ~~relative to a wild-type mouse~~.

35. (Currently Amended) The ~~transgenic~~ mouse of claim ~~1 32, 49, and 52~~, wherein the phenotype of said mouse is further characterized by ~~blepharitis~~ blepharitis ~~relative to a wild-type mouse~~.

36. (Currently Amended) The ~~transgenic~~ mouse of claim ~~1 32, 49, and 52~~, wherein the phenotype of said mouse is further characterized by interstitial pneumonitis ~~relative to a wild-type mouse~~.

37. (Currently Amended) The ~~transgenic~~ mouse of claim ~~1, 32, 49, and 52~~, wherein said mouse further displays an increase in peripheral T cells ~~relative to a wild-type mouse~~.

38. (Currently Amended) The ~~transgenic~~ mouse of claim 37, wherein said peripheral T cells of the mouse have a memory/activated phenotype characterized by decreased levels of Mel-14 and CD45RB, and increased levels of CD44 and CD69 relative to those of a wild-type mouse.

39. (Canceled)

40. (Currently Amended) The ~~transgenic~~ mouse of claim ~~139~~, wherein ~~said mouse displays the peripheral T cells of the mouse display~~ defective apoptosis relative to those of a wild-type mouse.

41. (Currently Amended) The ~~transgenic~~ mouse of claim ~~1, 32, 49, and 52~~, wherein ~~said mouse displays the peripheral T cells of the mouse display~~ increased Th2 cytokine production relative to those of a wild-type mouse.

42. (Currently Amended) The ~~transgenic~~ mouse of claim 41, wherein said Th2 cytokine is IL-4.

43. (Canceled)

44. (Currently Amended) The ~~transgenic~~ mouse of claim ~~43-1~~, wherein said mouse exhibits a higher level of antibodies having the immunoglobulin isotypes ~~are~~ IgG1 and IgE.

45. (Currently Amended) A method for identifying a test compound that modulates ~~immune~~ Th2 cell activation via a pathway that does not ~~involve~~ directly modulate NFATp or NFAT4 comprising:

a) administering said test compound to a first ~~transgenic~~ mouse comprising a genome deficient in NFATp and NFAT4;

b) administering an appropriate control compound to a second ~~transgenic~~ mouse comprising a genome deficient in NFATp and NFAT4, wherein the ~~phenotype~~ phenotypes of the first ~~transgenic~~ mouse and the second ~~transgenic~~ mouse ~~is~~ are characterized by increased Th2 cytokine production[[,]]; and

c) evaluating Th2 cell activity in said first ~~transgenic~~ mouse relative to Th2 cell activity in said second ~~transgenic~~ mouse ~~to thereby~~ wherein a change in Th2 cell activity in said first mouse relative to Th2 cell activity said second mouse identify identifies a compound that as one that regulates immune Th2 cell activation via a pathway that does not involve directly modulate NFATp or NFAT4.

46.-48. (Canceled)

49. (Currently Amended) A method for producing a ~~transgenic~~ mouse lacking NFATp and NFAT4, wherein said mouse exhibits a non-wildtype phenotype characterized by increased Th2 cytokine production relative to a corresponding wild-type mouse, comprising:

(~~1a~~) introducing an exogenous DNA molecule comprising at least a portion of a NFATp gene into a mouse embryonic stem cell ~~such that~~ to create a first modified stem cell in which the ~~wild-type endogenous~~ NFATp gene of the embryonic stem cell is functionally disrupted;

(~~2b~~) introducing said ~~transgenic mouse embryonic~~ first modified stem cell into a ~~pseudopregnant~~ mouse such that said ~~pseudopregnant~~ mouse produces at least one offspring comprising a functionally disrupted NFATp gene;

(~~3c~~) introducing an exogenous DNA molecule comprising at least a portion of a NFAT4 gene into a mouse embryonic stem cell to create a second modified stem cell in which ~~such that~~ the ~~wild-type endogenous~~ NFAT4 gene of the embryonic stem cell is functionally disrupted;

([[4]]d) introducing said ~~transgenic mouse embryonic~~ second modified stem cell into a ~~pseudopregnant~~ mouse such that said ~~pseudopregnant~~ mouse produces at least one offspring comprising a functionally disrupted NFAT4 gene; and

(5e) mating said at least one offspring with a functionally disrupted NFATp gene with said at least one offspring with a functionally disrupted NFAT4 gene and identifying subsequent offspring with both a functionally disrupted NFATp gene and a functionally disrupted NFAT4 gene to thereby produce a mouse lacking NFATp and NFAT4 which exhibits a non-wildtype phenotype characterized by increased Th2 cytokine production relative to a wild-type mouse.

50. (Currently Amended) ~~A mouse transgenic~~ An isolated cell from the mouse of claim 1 comprising a disrupted NFATp gene and a disrupted NFAT4 gene.

51. (Currently Amended) The mouse ~~transgenic~~ cell of claim 50, wherein said cell is selected from the group consisting of ~~fertilized egg cells~~, embryonic stem cells and lymphoid cells.

52. (Currently Amended) A method for producing a ~~transgenic~~ mouse with a functionally disrupted NFATp gene and a functionally disrupted NFAT4 gene, wherein said mouse exhibits a non-wildtype phenotype characterized by increased Th2 cytokine production, comprising:

mating a ~~transgenic~~ mouse ~~with~~ having a functionally disrupted NFATp gene with a ~~transgenic~~ mouse ~~with~~ having a functionally disrupted NFAT4 gene and identifying subsequent progeny with both a functionally disrupted NFATp gene and a functionally disrupted NFAT4 gene, to thereby produce a ~~transgenic~~ mouse with a functionally disrupted NFATp gene and a functionally disrupted NFAT4 gene that exhibits a non-wildtype phenotype characterized by increased Th2 cytokine production.

53. (New) The mouse of claim 1, wherein the mouse is further characterized by:

- (a) blepharitis;
 - (b) interstitial pneumonitis;
 - (c) splenomegaly and lymphadenopathy; and
 - (d) increased levels of serum IgG1 and IgE
- relative to a wildtype mouse.

54. (New) A mouse comprising in its genome a first exogenous DNA molecule that functionally disrupts a NFATp gene of said mouse and a second exogenous DNA molecule that functionally disrupts a NFAT4 gene of said mouse, wherein said mouse exhibits a non-wildtype phenotype characterized by increased Th2 cytokine production, blepharitis, interstitial pneumonitis splenomegaly and lymphadenopathy, and increased levels of serum IgG1 and IgE, relative to a wildtype mouse.